VIEWPOINT

Nitrites for Urinary Tract Infection—Time to Say Goodbye?

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The urinary nitrite test is a long-standing component of the dipstick portion of the urinalysis, but it is time to question its relevance in distinguishing urinary tract infection (UTI) from asymptomatic bacteriuria, and thus in guidance of antibiotic treatment decisions. Asymptomatic bacteriuria was initially recognized in the 1950s, but management was rarely discussed in the literature before a 2005 Infectious Diseases Society of America clinical practice guideline and a 2019 update.[1] Asymptomatic bacteriuria occurs in both adults and children and is defined as the presence of 10^8 CFU/L or greater in a voided urine specimen without signs or symptoms attributable to UTI.[1] Criteria for diagnosis of UTI are not uniform, but nearly all agree that there need to be compatible signs and symptoms, urinalysis, and culture results. When symptoms are vague or patients are unable to describe them, clinicians often use urinalysis results to decide whether to treat with antibiotics.

Testing for urinary nitrites can be traced back to the early 1900s due to discoveries made by Robert Koch and were first associated with UTI in 1914.[2] Today, the urinary nitrite test continues to be a standard component of the macroscopic dipstick portion of the urinalysis assay.[3] Urine normally contains nitrates as waste by-products of dietary protein.[2] A positive nitrite dipstick test, indicated by a color change, indicates the presence of nitrate-reducing bacteria in the urine.[3] Bacteria that possess the nitrate reductase enzyme include the most commonly implicated organisms causing UTI, namely *Escherichia coli* and *Klebsiella* species; however, this enzyme is notably absent in other urinary pathogens, including *Acinetobacter* and *Enterococcus* species.[3] There can be false-negative results with pathogens that have the enzyme since it is speculated that organisms must remain in the bladder for approximately 4 hours to produce detectable nitrites.[3] The question is whether the presence of bacteriuria, indicated by a positive nitrite test, can assist clinicians in deciding whether to start empirical antibiotics.

In an American Academy of Pediatrics statement on UTI in children aged up to 24 months, a positive nitrite test is stated to be "specific for UTI."[4] This statement is based on a small collection of studies from more than 30 years ago that confirm the ability of nitrites to detect bacteriuria; at that time, UTI was defined as a single culture positive for a urinary pathogen.[4] This definition ignores the fact that bacteriuria can be asymptomatic or the result of a contaminated urine sample. A 2019 meta-analysis reported similar diagnostic performance of nitrites for UTI in children in this age group, again not requiring symptoms for the practical reason that it is rarely possible to ascertain symptoms in young children.[5] A 2024 guidance paper on vesicoureteral reflux also stated that nitrites had a 99% specificity for UTI, and again UTI was defined by laboratory tests with no requirement for the presence of symptoms.[6] In summary, although the pediatric literature often quotes nitrites as being specific for UTI, the definition of UTI only specifies bacteriuria, encompassing asymptomatic bacteriuria and contaminated samples in addition to UTI.

In adults, current guidelines do not comment on the utility of urinary nitrites for the diagnosis of UTI. The most robust examination of the literature informing the use of nitrites in adults comes from a meta-analysis in 2004 investigating nitrites and leukocyte esterase as diagnostic predictors of UTI.[7] Although the authors concluded that nitrites had a high positive predictive value and specificity for UTI, the definition of UTI again included both symptomatic and asymptomatic bacteriuria. Importantly, the authors noted that nitrites seemed to perform better as predictors of asymptomatic than of symptomatic bacteruria.[7]

Urinary nitrite testing introduces diagnostic confusion without adding value with regard to the decision to treat. In a symptomatic patient who has significant pyuria without nitrites, treatment is warranted, as there may be a pathogen present that lacks the nitrate reductase enzyme. Conversely, in a symptomatic patient who lacks pyuria and has nitrites, treatment is usually not indicated, as the nitrites could be produced by contaminants in the urine sample or from asymptomatic bacteriuria. Furthermore, in an asymptomatic patient, nitrite positivity may lead to reflex urine microscopy that in turn may detect bacteriuria due to contamination or asymptomatic bacteriuria, and this may increase the probability of inappropriately prescribing antibiotics. We acknowledge that in resource-limited settings where urine cultures and/or microscopy are unavailable, it may be reasonable to use the urine dipstick test to assist clinical diagnosis, with emphasis on the presence of pyuria over urinary nitrites.

Use of the nitrite test to guide antibiotic selection in a symptomatic patient is also problematic due to the intrinsic limitations of the nitrite test. In a patient with a true UTI, a negative nitrite result could be due either to a Gram-positive bacteriuria or a non-nitrate–reducing Gram-negative bacteriuria (such as *Acinetobacter* species). However, a positive nitrite result might be useful in the rare situation when considering empirical coverage for Gram-positive organisms, such as an ill patient with a recent enterococcal UTI; this positive nitrite might reassure the clinician that enterococcal coverage would not be necessary.

In conclusion, urinary nitrites provide diagnostic redundancy in confirming the presence of bacteriuria at best and promote the unnecessary use of antibiotics in asymptomatic patients at worst. Future research should examine the effects of suppressing the nitrite result from the urinary dipstick to determine the downstream effects on antimicrobial prescribing. Additionally, improving diagnostic techniques for distinguishing true UTI from

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asymptomatic bacteriuria should be a focus of future research. Our viewpoint is that urinary nitrites should no longer be used for the diagnosis of UTI in pediatric or adult patients. Clinical assessment of signs and symptoms in combination with the presence or absence of pyuria provides an appropriate approach in deciding when to start empirical antibiotics for UTIs.

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